

## AMENDMENTS TO THE CLAIMS

Claim 1 (original). A modified molecule having the biological activity of bryodin 1 and being substantially non-immunogenic or less immunogenic than any non-modified molecule having the same biological activity in an individual when used *in vivo*, wherein the said loss of immunogenicity is achieved by removing one or more T-cell epitopes derived from the originally non-modified molecule and said T-cell epitopes are MHC class II ligands or peptide sequences which show the ability to stimulate or bind T-cells via presentation on class II.

Claim 2 (original). A byrodin 1 molecule of claim 1, wherein the removing of said T-cell epitopes are achieved by replacing 1 – 9 amino acid residues.

Claim 3 (cancelled).

Claim 4 (currently amended). A byrodin 1 molecule of claim 1 [[or 2]], wherein said T-cell epitopes are located within the strings of contiguous amino acid residues termed as R1 – R5 encompassing residues 46-66; 88-102; 112-135; 136-162 ~~and 178-204~~ and 178-204 of the wild-type byrodin 1 sequence (SEQ ID NO: 1).

Claims 5-16 (cancelled).

Claim 17 (new). A polypeptide having the biological activity of human bryodin 1, the polypeptide comprising the amino acid residue sequence of wild-type human bryodin 1, SEQ ID NO: 1, and including at least one amino acid residue substitution in an epitope region of SEQ ID NO: 1, the amino acid residue substitution rendering the polypeptide less immunogenic to a human than wild-type human bryodin 1.

Claim 18 (new). The polypeptide of claim 17 wherein the at least one amino acid residue substitution comprises one to nine amino acid residue substitutions in SEQ ID NO: 1.

Claim 19 (new). The polypeptide of Claim 17 wherein the at least one amino acid residue substitution is a substitution in at least one epitope region of SEQ ID NO: 1 selected from the group consisting of amino acid residues 46-66 of SEQ ID NO: 1, amino acid residues 88-102 of SEQ ID NO: 1, amino acid residues 112-135 of SEQ ID NO: 1, amino acid residues 136-162 of SEQ ID NO: 1, and amino acid residues 178-204 of SEQ ID NO: 1.

Claim 20 (new). The polypeptide of claim 19 wherein the at least one amino acid residue substitution comprises one to nine amino acid residue substitutions in SEQ ID NO: 1.

Claim (21 (new). A polypeptide comprising the amino acid residue sequence of SEQ ID NO: 7:

DVSFRLSGATTTSYGVFIKNLREALPYERKVYNIPLLRSSISGSGRY<sup>1</sup>X<sup>2</sup>LX<sup>3</sup>LT<sup>4</sup>X<sup>5</sup>ADET<sup>6</sup>SVAX<sup>7</sup>DX<sup>8</sup>TNVYIMGYLAGDVSYFFNEASATEAAK<sup>9</sup>X<sup>10</sup>FKDAKKK<sup>11</sup>TLPYSGNYER<sup>12</sup>QT<sup>13</sup>AX<sup>14</sup>X<sup>15</sup>X<sup>16</sup>X<sup>17</sup>ENX<sup>18</sup>PLGX<sup>19</sup>PAX<sup>20</sup>DSAX<sup>21</sup>TTX<sup>22</sup>YX<sup>23</sup>X<sup>24</sup>TASSAASAX<sup>25</sup>X<sup>26</sup>X<sup>27</sup>X<sup>28</sup>IQSTAESARYKFIEQQIGKRVDTFLP  
SLATX<sup>29</sup>SX<sup>30</sup>ENNWSAX<sup>31</sup>SX<sup>32</sup>QX<sup>33</sup>QX<sup>34</sup>ASTNNGQFESPVVLIDGNNQRV SITNASARVVTSNIALLLNRN  
NIAAIGEDISMTLIGFEHGLYGI (SEQ ID NO: 7)

wherein

X<sup>1</sup> is A, G or P; X<sup>2</sup> is M, A, G, P or I; X<sup>3</sup> is A, G or P; X<sup>4</sup> is P or Y;

X<sup>5</sup> is T or S; X<sup>6</sup> is P; X<sup>7</sup> is A, P or G; X<sup>8</sup> is A, P or G;

X<sup>9</sup> is A, P, G, H, D, E, N, Q, K, R, S or T; X<sup>10</sup> is A, P or G; X<sup>11</sup> is A, P or G;

X<sup>12</sup> is A, P, S, T, H or K; X<sup>13</sup> is T; X<sup>14</sup> is H; X<sup>15</sup> is S;

X<sup>16</sup> is A, S, T, P, N, D, E, G, H, K or Q; X<sup>17</sup> is T; or P;

X<sup>19</sup> is A, I, F, G, M, P, V, W or Y; X<sup>20</sup> is F, P or W; X<sup>21</sup> is A, P or G;

X<sup>22</sup> is G, A or P; X<sup>23</sup> is G, A or P; X<sup>24</sup> is A, P or G; X<sup>25</sup> is A, P, G, S or T;

X<sup>26</sup> is A, I, M, S, T, P or G; X<sup>27</sup> is A, G or P;

X<sup>28</sup> is S, A, G, P, T, H, D, N, Q, K or R;

X<sup>29</sup> is T, A, G, S, P, H, K, R, D, E, N or Q;

X<sup>30</sup> is A, G, S, T, P, K, R, H, D, E, N or Q; X<sup>31</sup> is Q;

X<sup>32</sup> is H, D, E, F, L, N, P, S, W or Y;

X<sup>33</sup> is T, A, G, P, D, E, H, K, R, N, Q, S or T; and X<sup>34</sup> is D;

with the proviso that the variable amino acid residues  $X^1$  through  $X^{34}$  do not simultaneously have the following combination of identities:

$X^1 = T$ ,  $X^2 = L$ ,  $X^3 = H$ ,  $X^4 = N$ ,  $X^5 = Y$ ,  $X^6 = I$ ,  $X^7 = V$ ,  $X^8 = V$ ,  $X^9 = F$ ,  $X^{10} = V$ ,  
 $X^{11} = V$ ,  $X^{12} = L$ ,  $X^{13} = A$ ,  $X^{14} = G$ ,  $X^{15} = K$ ,  $X^{16} = I$ ,  $X^{17} = R$ ,  $X^{18} = I$ ,  $X^{19} = L$ ,  $X^{20} = L$ ,  $X^{21} = I$ ,  $X^{22} = L$ ,  
 $X^{23} = Y$ ,  $X^{24} = Y$ ,  $X^{25} = L$ ,  $X^{26} = L$ ,  $X^{27} = V$ ,  $X^{28} = L$ ,  $X^{29} = I$ ,  $X^{30} = L$ ,  $X^{31} = L$ ,  $X^{32} = K$ ,  $X^{33} = I$ , and  $X^{34} = I$ .

Claim 22 (new). The polypeptide of claim 21 wherein  $X^1$  is A,  $X^2$  is M,  $X^3$  is A,  $X^4$  is P,  $X^5$  is T,  $X^6$  is P,  $X^7$  is A,  $X^8$  is A,  $X^9$  is A,  $X^{10}$  is A,  $X^{11}$  is A,  $X^{12}$  is A,  $X^{13}$  is T,  $X^{14}$  is H,  $X^{15}$  is S,  $X^{16}$  is A,  $X^{17}$  is T,  $X^{18}$  is A,  $X^{19}$  is A,  $X^{20}$  is F,  $X^{21}$  is A,  $X^{22}$  is G,  $X^{23}$  is G,  $X^{24}$  is A,  $X^{25}$  is A,  $X^{26}$  is A,  $X^{27}$  is A,  $X^{28}$  is S,  $X^{29}$  is T,  $X^{30}$  is A,  $X^{31}$  is Q,  $X^{32}$  is H,  $X^{33}$  is T and  $X^{34}$  is D.

Claim 23 (new). The polypeptide of claim 21 wherein the polypeptide exhibits, in a biological assay of induced cellular proliferation of human T-cells, a stimulation index (SI) having a value less than 2 and less than the SI of wild-type human bryodin 1, when the polypeptide and wild-type human bryodin 1 are tested in parallel using cells from the same donor, and wherein the SI is determined as the value of cellular proliferation obtained from T-cells stimulated with the polypeptide or bryodin 1, divided by the value of cellular proliferation determined in control T-cells not exposed to the polypeptide or bryodin 1, respectively.

Claim 24 (new). A pharmaceutical composition comprising a polypeptide of claim 17 together with a material selected from the group consisting of a carrier, a diluent, and an excipient.

Claim 25 (new). A pharmaceutical composition comprising a polypeptide of claim 21 together with a material selected from the group consisting of a carrier, a diluent, and an excipient.

Claim 26 (new).        An isolated polypeptide consisting of an amino acid residue sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6.

Claim 27 (new).        An isolated polypeptide consisting of any one of the amino acid residues sequences depicted in FIGURE 1.

Claim 28 (new).        An isolated polypeptide consisting of any one of the amino acid residues sequences depicted in FIGURE 2.

Claim 29 (new).        An isolated deoxyribonucleic acid encoding a polypeptide of claim 17.

Claim 30 (new).        An isolated deoxyribonucleic acid encoding a polypeptide of claim 21.